

Normal cellular response to chemoattractant signaling.

00000000000000000000000000000000

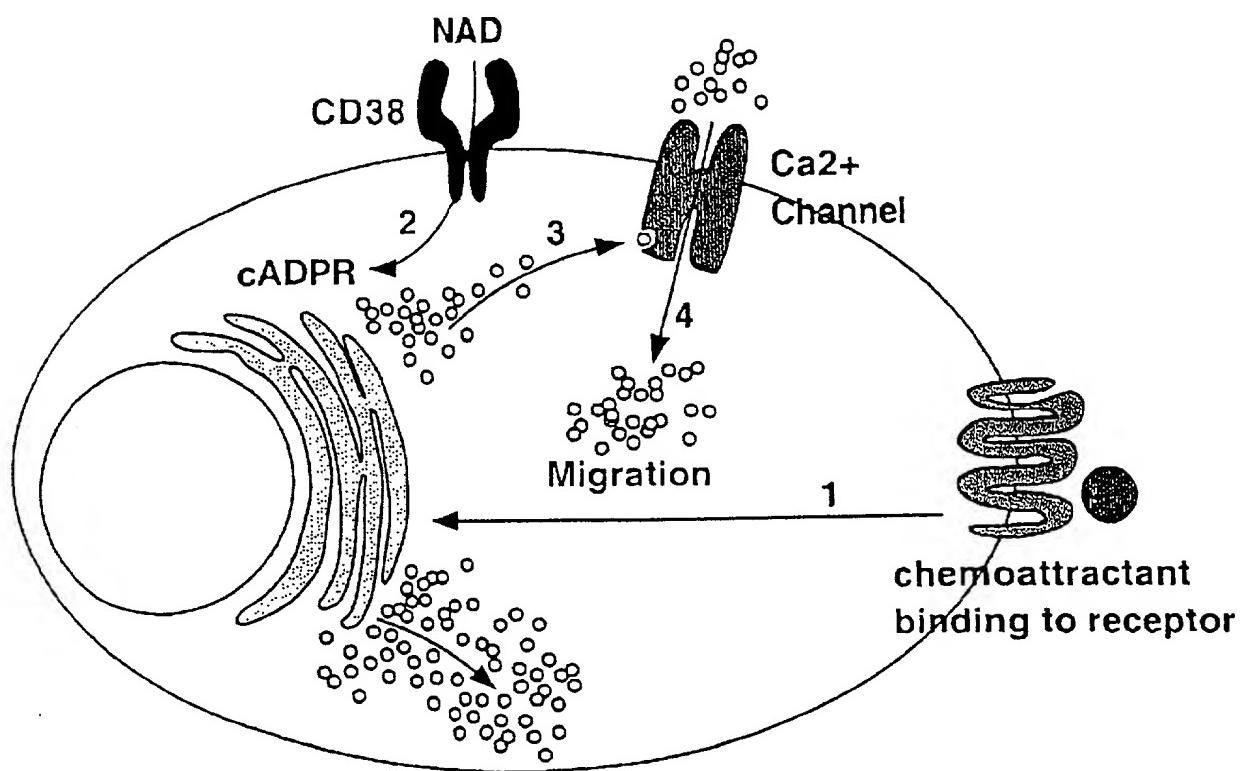


Figure 1

Inhibitors of cADPR production
by CD38 prevent capacitative
Ca²⁺ entry and chemoattractant
induced migration

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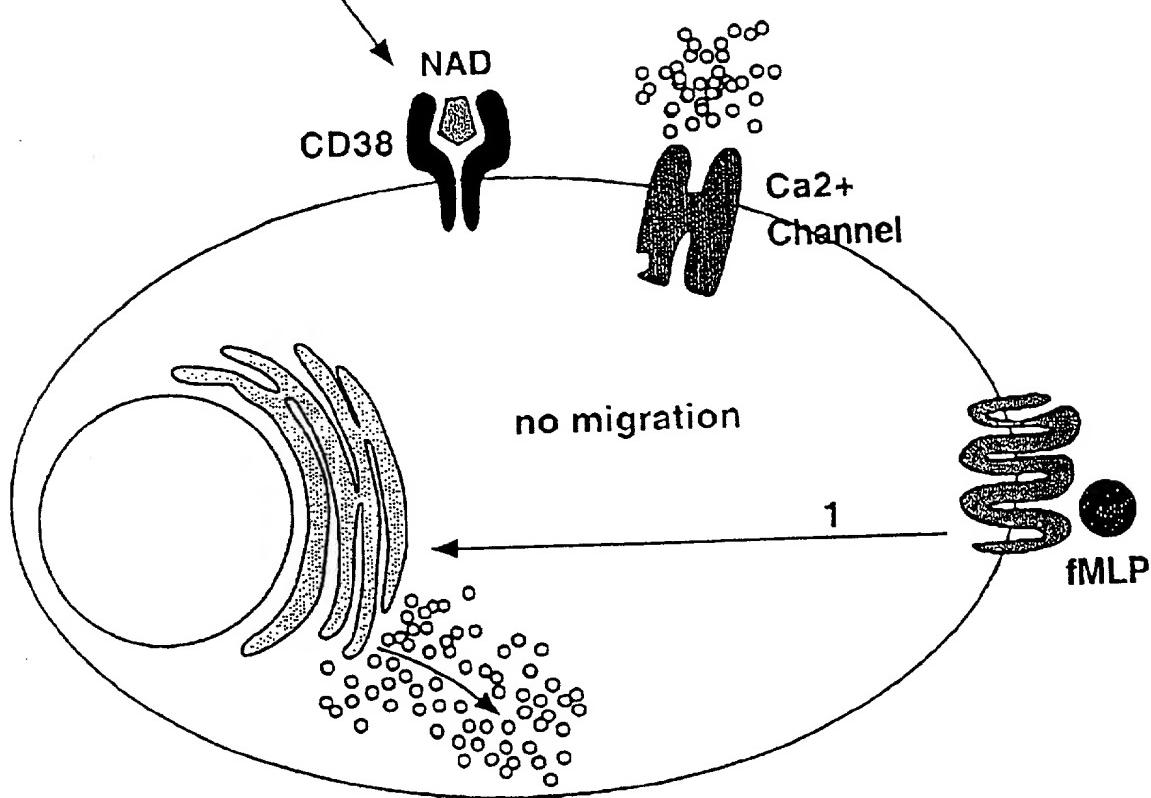


Figure 2

Proteins that regulate CD38 enzyme activity (screens will identify compounds that activate or inactivate these proteins)

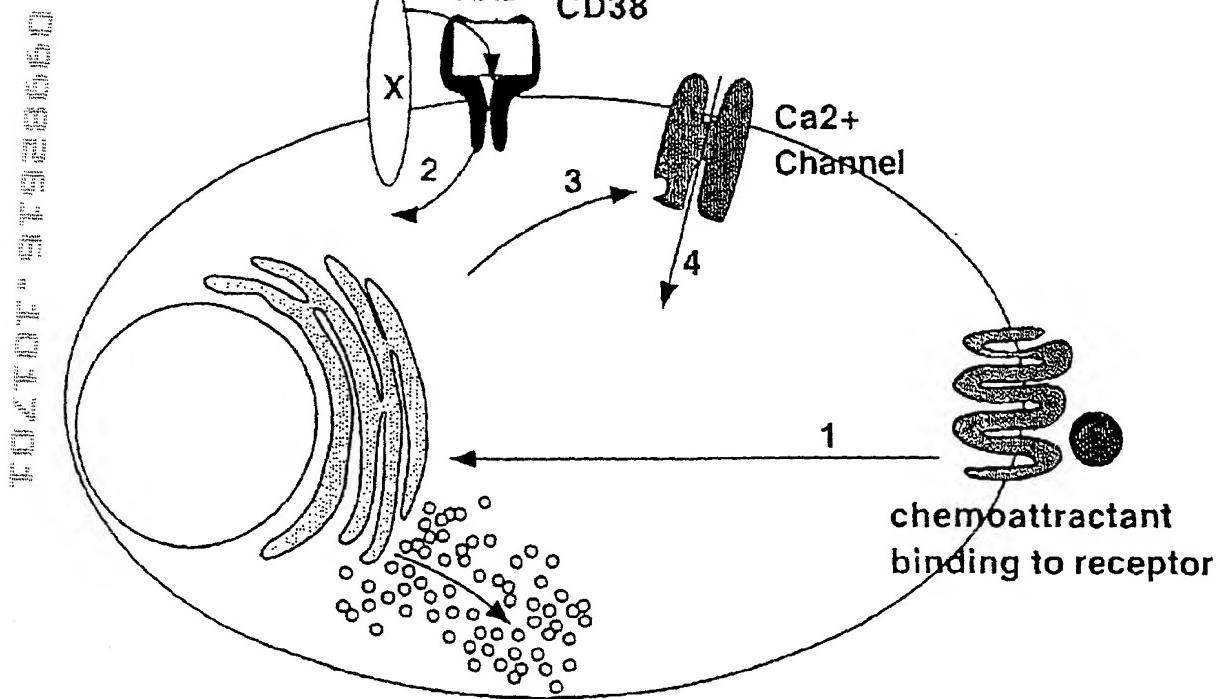


Figure 3

Proteins that regulate CD38 expression (screens will identify compounds that activate or inactivate these proteins)

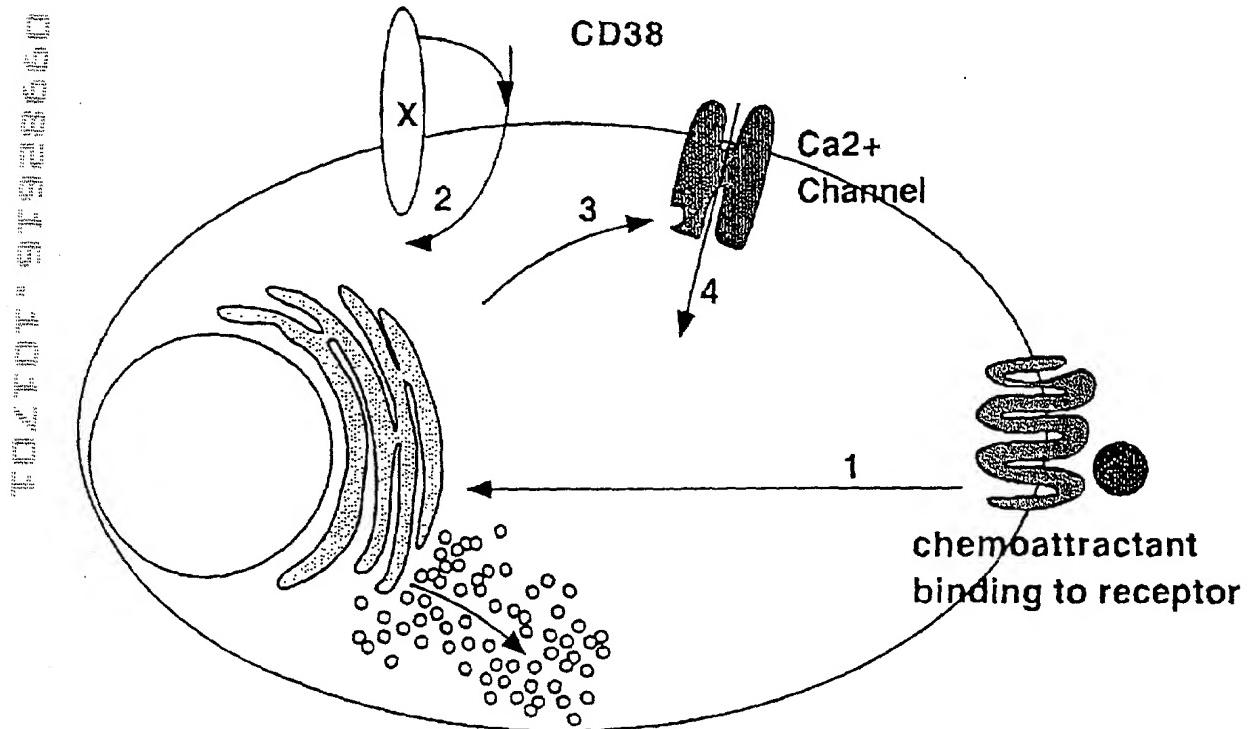


Figure 4

Alternative substrates for CD38 may generate inhibitors of cADPR and prevent capacitative Ca^{2+} release

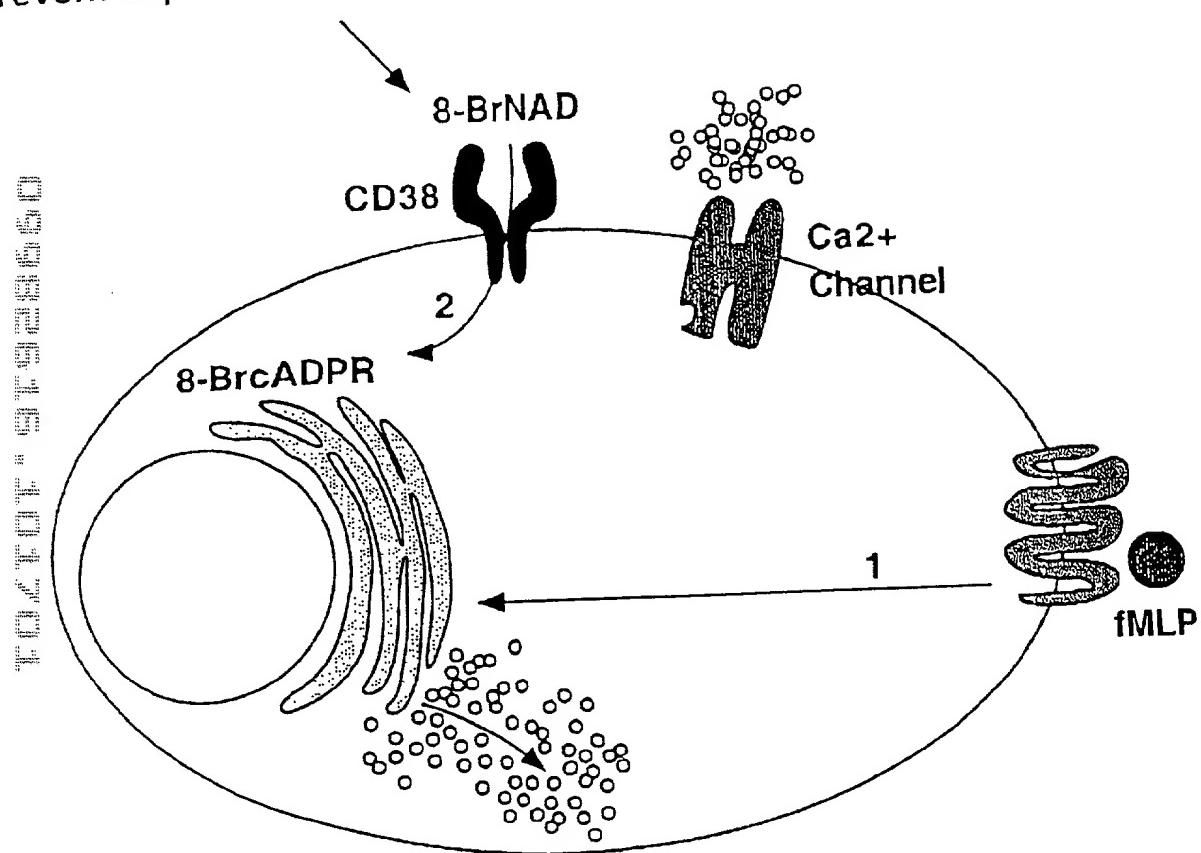


Figure 5

Inhibitors of cADPR binding
block capacitative Ca^{2+} influx

PROTOTYPING FOR 2000

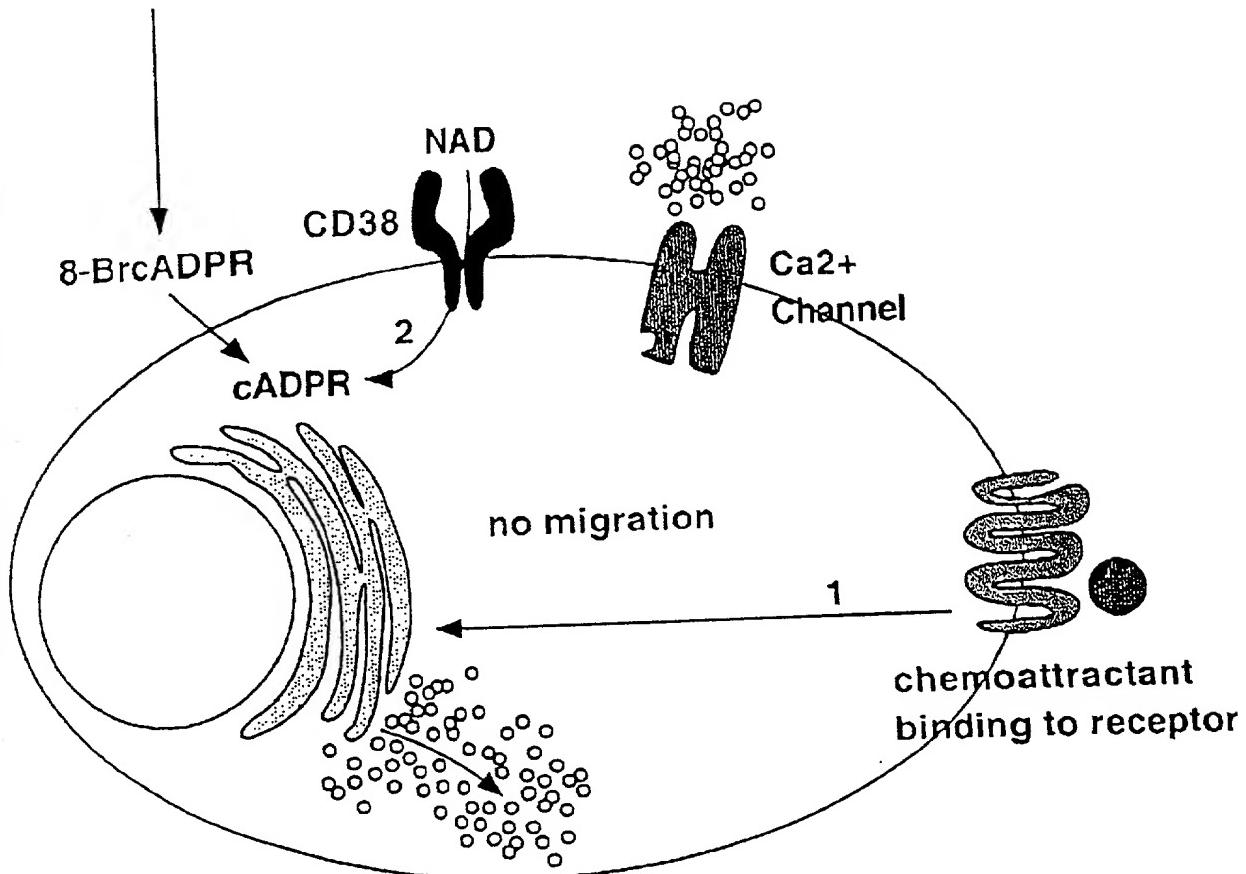


Figure 6

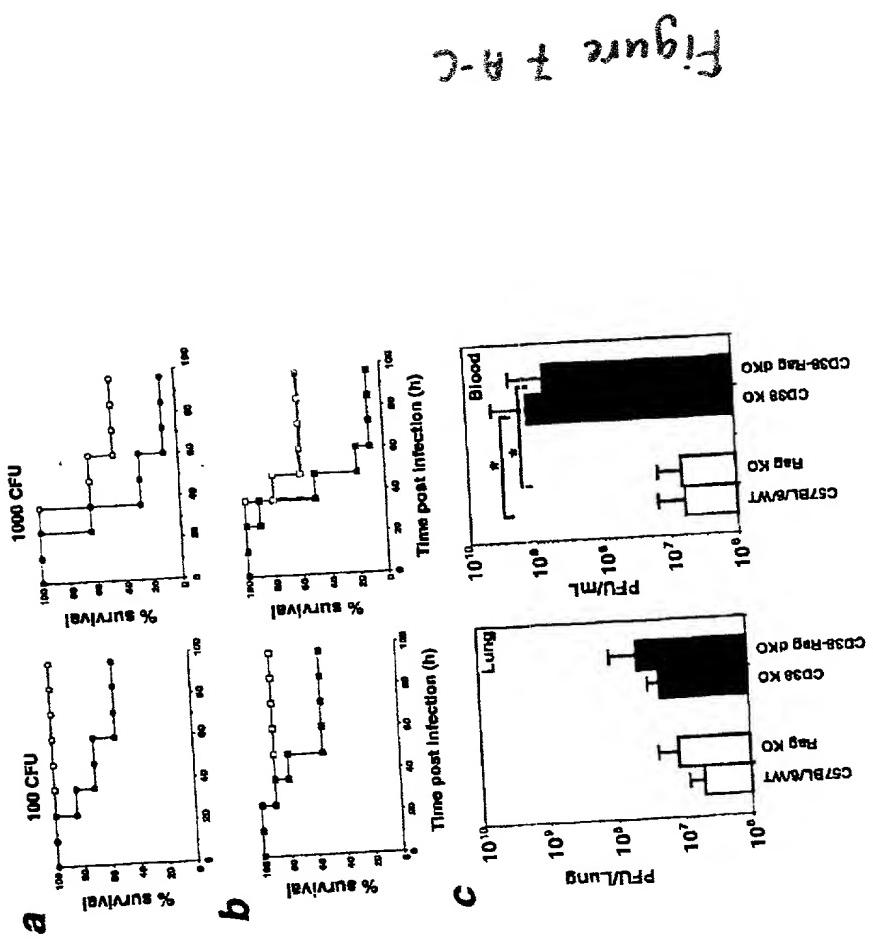
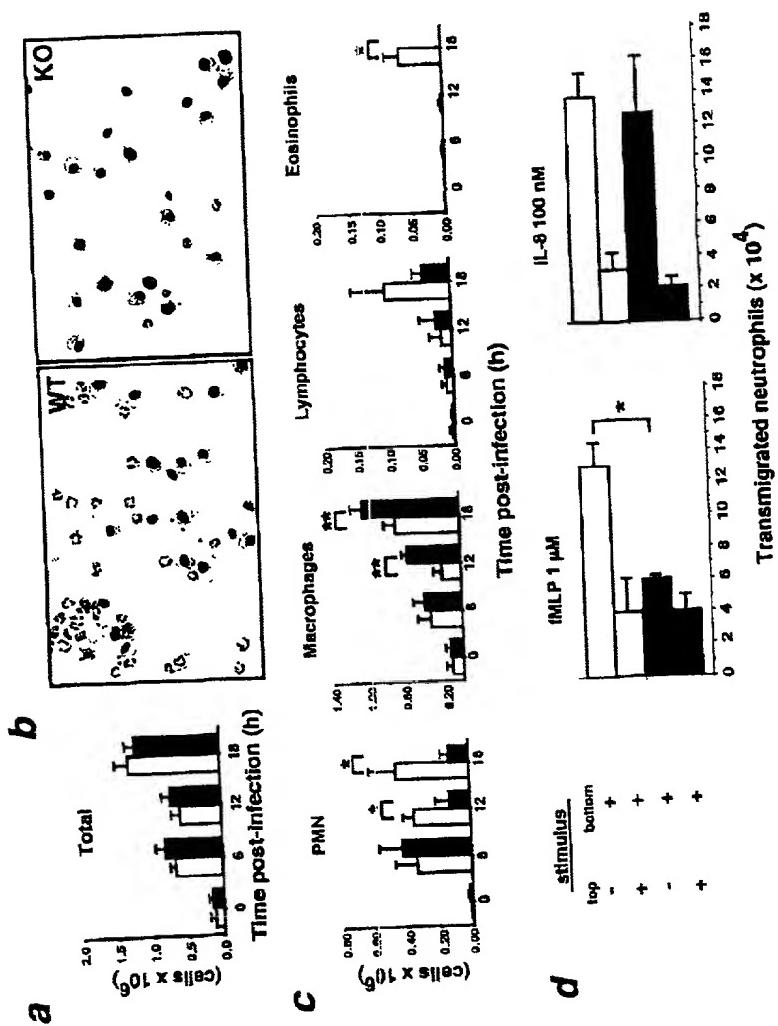
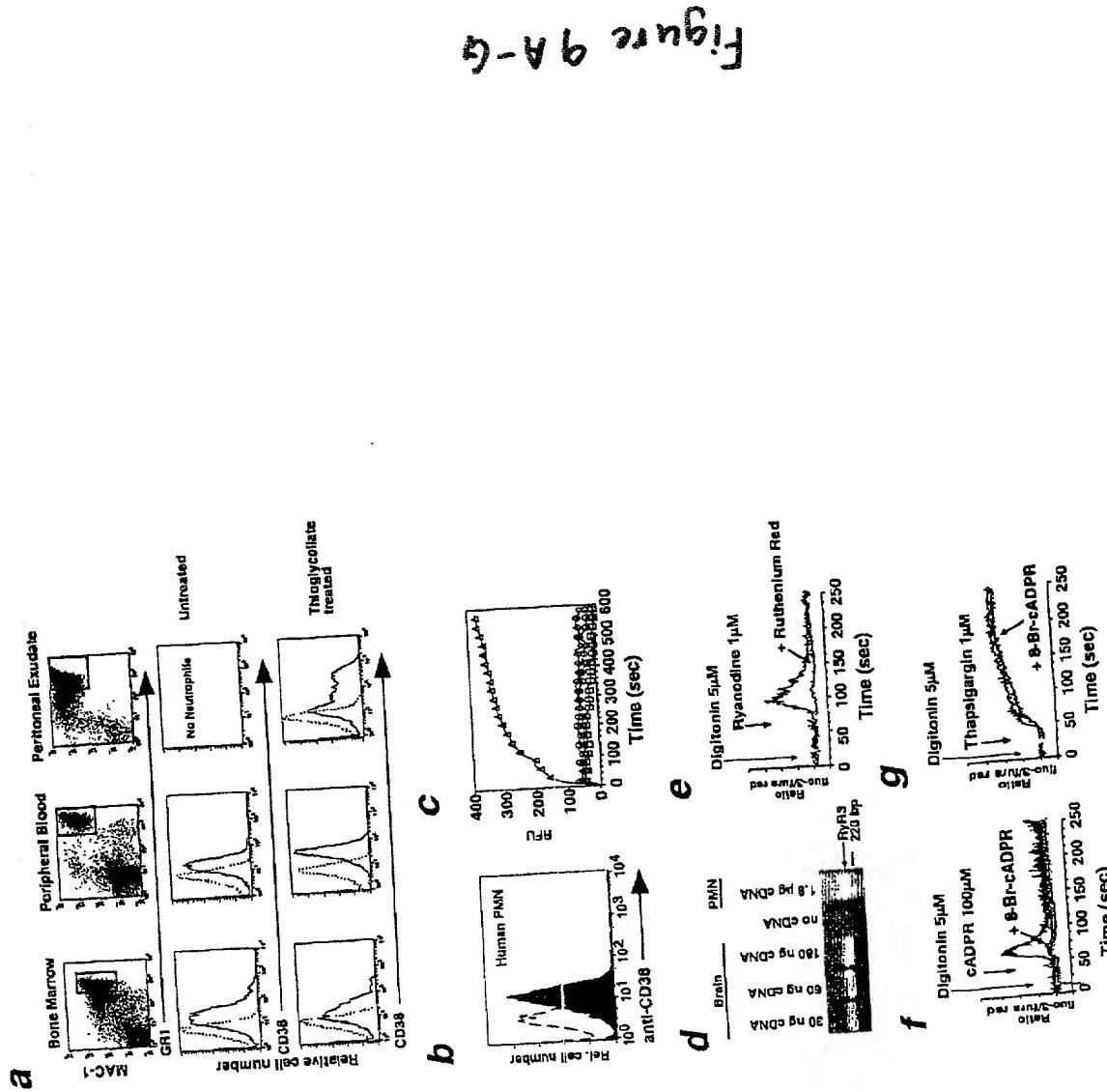


Figure 8 A-D





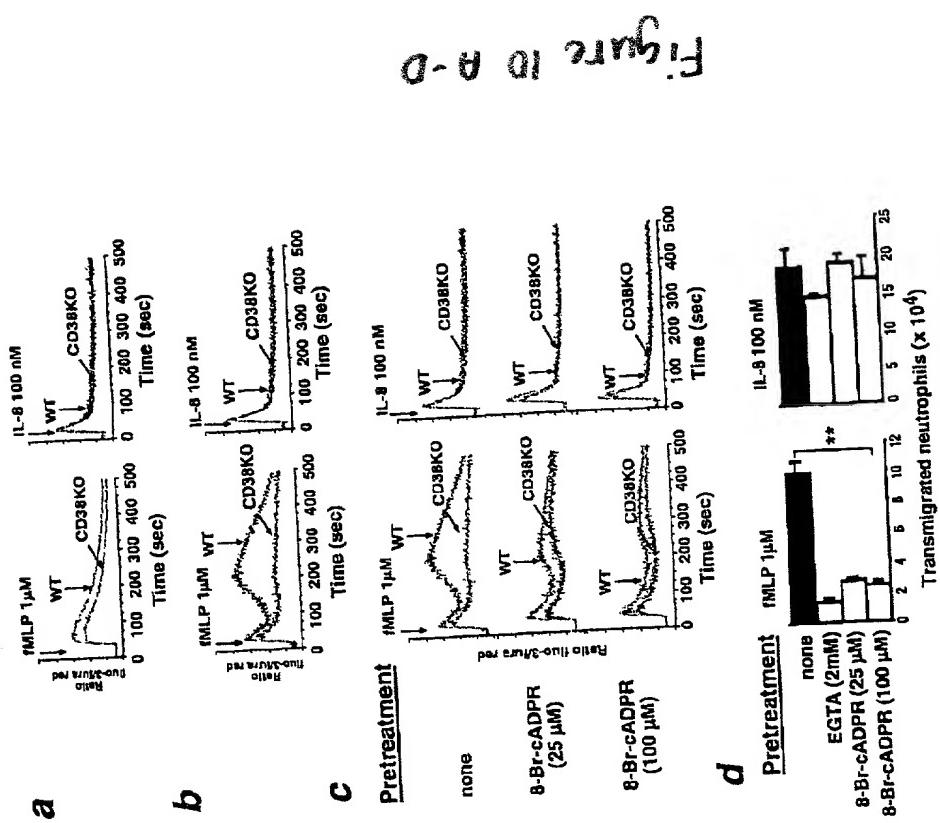
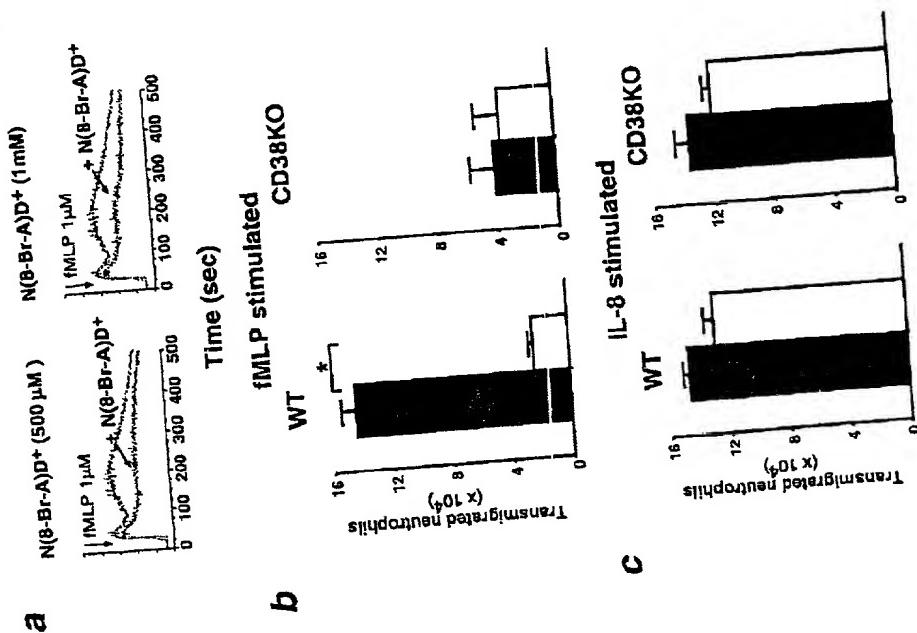


Figure 11 Ac



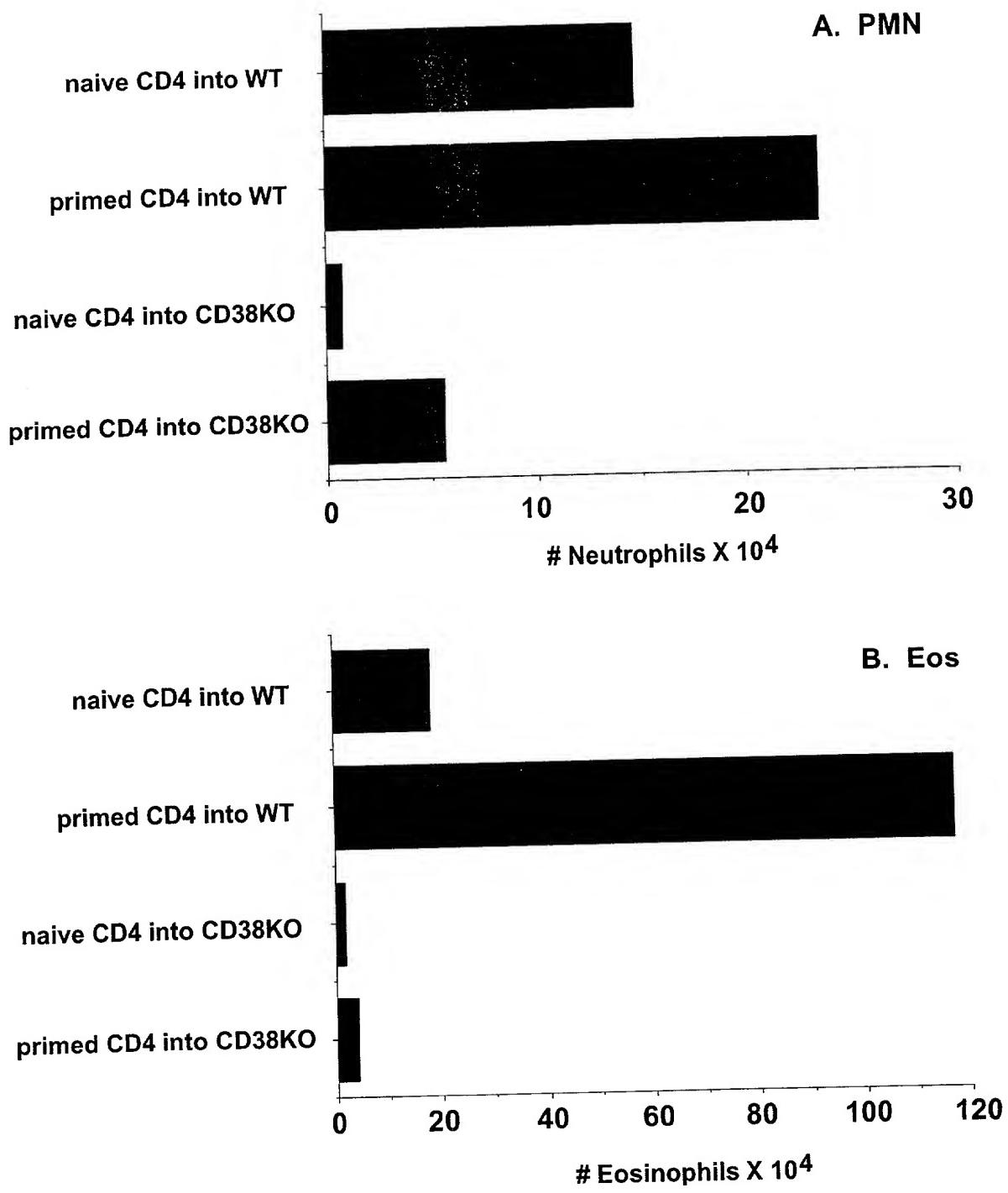


Figure 12

Figure 13A

Consensus	GGAAAGAACG TAGACATATA TTGTTATATA GATTGTTCA GTTATTTTTC	50
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	GGAAAGAACG TAGACATATA TTGTTATATA GATTGTTCA GTTATTTTTC	50
Consensus	ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA	100
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	ACAATCTTTT AATTCAAATA ATGATGAACG TAATATTGTT TCTTACTTTA	100
Consensus	TCAAATATTT TTGTCTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG	150
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	TCAAATATTT TTGTCTTAA CTCTGCACAA CATCAAATAA ACTTACTTAG	150
Consensus	TGAAATAGTA CAATCACGAT GTACTCAGTG GAAGGTTGAA CATGGAGCTA	200
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	TGAAATAGTA CAATCACGAT GTACTCAGTG GAAGGTTGAA CATGGAGCTA	200
Consensus	CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTGAAAG CATTACTT	250
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	CTAATATAAG TTGTAGTGAG ATCTGGAATT CATTGAAAG CATTACTT	250
Consensus	TCAACTCATA CTAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA	300
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	TCAACTCATA CTAATCAGC ATGTGTTATG AAATCAGGGT TATTCGATGA	300
Consensus	TTTGTTTAT CAATTGTTG AATTGGAACA ACAACAACAA CAGCGACACC	350
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	TTTGTTTAT CAATTGTTG AATTGGAACA ACAACAACAA CAGCGACACC	350
Consensus	ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT	400
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	ACACAATTCA AACGGAACAA TACTTCCATT CTCAAGTGAT GAACATCATT	400
Consensus	CGTGGATGT GTAACGTCT TGGAGTATGT CGTTCTCTAG AAACTACATT	450
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	-----	
SM38	CGTGGATGT GTAACGTCT TGGAGTATGT CGTTCTCTAG AAACTACATT	450

Figure 13B

Consensus	TCCAGGATAT CTGTTGATG AATTGAATTG GTGTAATGGC AGTTAACAG	500
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	TCCAGGATAT CTGTTGATG AATTGAATTG GTGCAATGGC AGTTAACAG	79
SM38	TCCAGGATAT CTGTTGATG AATTGAATTG GTGTAATGGC AGTTAACAG	500
Consensus	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	550
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	129
SM38	GCAACACAAA ATACGGGACT GTATGTGGAT GCGATTATAA AAGTAATGTT	550
Consensus	GTTCATGCCT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	600
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	GTTCATGCCT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	24
SM38	GTTCATGCCT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	179
Consensus	GTTCATGCCT TCTGGCAAAG TGCTTCGGCT GAGTATGCCA GGAGAGCATC	600
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
SM38	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	74
Consensus	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	229
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
SM38	TGGTAACATC TTTGTGGTAC TGAATGGCTC GGTCAAAGCT CCATTTAATG	650
Consensus	AAAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG	700
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	AAAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG	123
SM38	AAAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG	279
Consensus	AAAAATAAAAC TTTTGGAAAA ATAGAACTAC CATTGGTTAA AACATCCTCG	699
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTGGAA GATGAAATA	750
SM38	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTGGAA GATGAAATA	173
Consensus	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTGGAA GATGAAATA	280
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	A- AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTGGAA GATGAAATA	749
SM38	AGTACAACAA TTAACAGTGA AATTAGTTCA TAGTTGGAA GATGAAATA	749
Consensus	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	800
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	223
SM38	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	280
Consensus	ACCGACAAAC ATGTGAATCG TGGAGTCTGC AAGAACTTGC AAACAAGCTG	799
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	AACTCTGTAC ATATTCTTT TCGTTGCATT GACGATCCTT TAGAGTCAG	850
SM38	AACTCTGTAC ATATTCTTT TCGTTGCATT GACGATCCTT TAGAGTCAG	273
Consensus	AACTCTGTAC ATATTCTTT TCGTTGCATT GACGATCCTT TAGAGTCAG	280
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	AACTCTGTAC ATATTCTTT TCGTTGCATT GACGATCCTT TAGAGTCAG	849
SM38	AACTCTGTAC ATATTCTTT TCGTTGCATT GACGATCCTT TAGAGTCAG	849
Consensus	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTCAG	900
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTCAG	323
SM38	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTCAG	37
Consensus	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTCAG	280
EST AW017229 comp	-----	
EST AI067047 comp	-----	
EST N20756	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTCAG	899
SM38	ACATTATCAA TGCATTGAAA ATCCTGGCAA ACAACTATGT CAGTTTCAG	899

Figure 18C

Consensus	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTT TCCGCTAGTC	950
EST AW017229 comp	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTT TCCGCTAGTC	373
EST A1067047 comp	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTT TCCGCTAGTC	87
EST N20756	-----	280
SM38	CTTCGACGAG GTCAAACGTC GAGACATTAC TCATACTTT TCCGCTAGTC	949
Consensus	ATTTGTTAA CTTTTATAC TTCCATGAAT TGAAATAACT TTCAGAACT	1000
EST AW017229 comp	ATTTGTTAA CTTTTATAC TTCCATGAAT TGAAATAACT TTCAGAACT	423
EST A1067047 comp	ATTTGTTAA CTTTTATAC TTCCATGAAT TGAAATAACT TTCAGAACT	137
EST N20756	-----	280
SM38	ATTTGTTAA CTTTTATAC TTCCATGAAT TGAAATAACT TTCAGAACT	999
Consensus	AAACTTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGMCATTA	1050
EST AW017229 comp	AAACTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGCCATTA	473
EST A1067047 comp	AAACTTG-----	145
EST N20756	-----	280
SM38	AAACTTGAA CAGAGAAAGA GAACAATGAT AATAAAGGAA TAGGACATTA	1049

Figure 14

GGAAAGAACGTAGACATATATTGTTATAGATTGTTCACTTACAGTTTACAATCTTTAATTCAAATA
 E R T . T Y I V I . I C S V I F H N L L I Q I 70
 'ATGATGAACGTAATTGTTCTACTTATCAAATATTTGTCCTTAACTCTGCACAAACATCAAATAA
 M M N V I L F L T L S N I F V F N S A Q H Q I 140
 ACTTACTTAGTGAAATAGTACAATCACGATGTA CAGTGGAGGTTGAACATGGAGCTACTAATATAAG
 N L L S E I V Q S R C T Q W K V E H G A T N I S 210
 TTGAGATCTGGAATTCAATTGAAAGCATTTCAGTCAACTCATACTAAATCAGCATGTTATG
 C S E I W N S F E S I L L S T H T K S A C V M 280
 AAATCAGGGTTATCGATGATTTGTTATCAATTGTTGAATTGAAACAACAACAACAGCGACACC
 K S G L F D D F V Y Q L F E L E Q Q Q Q Q R H 350
 ACACAATTCAAACGGAACAATCTCCATTCTCAAGTGATGAAACATCATTGTTGAATGTTAAACGCT
 H T I Q T E Q Y F H S Q V M N I I R G M C K R L 420
 TGGAGTATGTCGTTCTAGAAAACATTTCCAGGATATGTTGATGAAATTGAAATTGGTGTAAATGGC
 G V C R S L E T T F P G Y L F D E L N W C N G 490
 AGTTAACAGGCAACACAAAATACGGGACTGTATGTTGATGCGATTATAAAAGTAATGTTGTTCATGCGT
 S L T G N T K Y G T V C G C D Y K S N V V H A 560
 TCTGGCAAAGTGTGCTGAGTATGCCAGGAGAGCATCTGGTAACATCTTGTTGACTGAATGGCTC
 F W Q S A S A E Y A R R A S G N I F V V L N G S 630
 GGTCAAAGCTCCATTAAATGAAAATAAAATTTGGAAAATAGAAACTACCATTGTTAAACATCCTCGA
 V K A P F N E N K T F G K I E L P L L K H P R 700
 GTACAACAATTAAACAGTGAAATTAGTTCATAGTTGAAAGATGTAATAACCGACAAACATGTGAATCGT
 V Q O L T V K L V H S L E D V N N R Q T C E S 770
 GGAGTCTGCAAGAACTTGCAAACAAAGCTGAACTCTGTACATATTCTTTCGTTGCATTGACGATCCTT
 W S L Q E L A N K L N S V H I P F R C I D D P L 840
 AGAGTTCAGACATTATCAATGCATGAAAATCTGGCAAACAAACTATGTCAGTTTCAGCTTCGACGAGG
 E F R H Y O C I E N P G K Q L C Q F S A S T R 910
 TCAAAACGTCGAGACATTACTCATACTTTCCGCTAGTCATTGTTAACTTTTATACTTCCATGAATT
 S N V E T L L I L F P L V I C L T F Y T S M N 980
 GAAATAACTTTCAAGAACTAAACTTGAACAGAGAAAAGAGAACATGATAATAAGGAATAGGACATTAA
 . N N F S E L N F E Q R K R T M I I K E . D I N 1050
 TGAAAAAAAAAAAAAA 1073
 E K K K K K K K

A.	Consensus	M.....L.....S.....I.....L.....RC.....	50
	Aplysia cd38p SM38p	MSPVAIVACV CLAVTLTRIS PSEAIFPTPE LQNVFLGRCK DYEITRYLT M---MNVLFL TLSNIFVFN S AQHQI---NL LSEIVQSRCQ WKVEH---	50 41
	ConsensusC...W..F.....K..C...G...DF.....	100
	Aplysia cd38p SM38p	LPRVKSDCRA LWTNFFKAES F---KAPCNL DLGSYKDFQQ RAQQTLPKNK -GATNISCSE IWSFESILL STHTIKSACVM KSGLFDDFVY QLFELEQQQQ	97 90
	Consensus*.....LE.T.PGY.....L.WC..	150
	Aplysia cd38p SM38p	VMFWSGVYDE --AHDF--- ADDGRKYI-- TIEDTLPGV MLNSIVWCQ QRHHTIQTEQ YFHSQVMNII RGMCKRLGVC RSLETTFPGV LFDELNWCG	138 140
	ConsensusVC....D....FW..A S..YA..A.GGS.	200
	Aplysia cd38p SM38p	RDKPGFNQK- VCPDFKDCPV QARESFNGTA SSSYAHSAEG DVTYMVDSN SLTGNTKYGT VC--GCDYKS NVVHAFWQSA SAEYARRASG NIFVVLNGS-	187 186
	Consensus*.....FGK.EPL.L....V.....H.L....C..SL	250
	Aplysia cd38p SM38p	PKVPAYRPD S FFGKYELPNL TNK-MTKVKV 1VLHQLGQKI I-EROGAGSL -VKAPFNENK TFGKIELPLU KHPRVQQLTV KLVSLEDVN NRQTCESWL	235 236
	Consensus	..L.....F.C..P.....C..NP....CQ.....	300
	Aplysia cd38p SM38p	LDLEMVVAKA KFGFDVENV KSVLFLLCAD NPNARECOLA KRYYRIA-- QEANKLNSV HIPFRCIDDP LEFRHYOCIE NPGKQLCQFS ASTRSNVETL	282 286
	Consensus	317
	Aplysia cd38p SM38p	----- LILFPLVICL TFYTSMN	282 303
B.	Consensus	M.....IL...L.....Q.	50
	Human CD38 SM38p	MANCEFSPVS GDKPCCRSLR RAQLCLGVSI LVLILVVLA VVPRWRQQW M----- MNVLFLTLS NIFVFN SAQ-	50 20
	ConsensusE.V..RC.....C...W..F....S.H.K.	100
	Human CD38 SM38p	SGPGTTKRFP ETVLARCVKY TEIHPMRHV DCQSVWDFAK GAFIS--RH ---HQINLLS EIVQSRCQW -KVEHGATNI SCSEIWNSFE SILLSTHTKS	97 66
	Consensus	.C.....YQ.....S.....	150
	Human CD38 SM38p	PQNITEED-- M QPLMKL GTQTVPCNKI L---LWSRI KDLAHQFTQV ACVMKSGLFD DFVYQLFELE QQQQQRHHTI QTEQYFHSQV MNII RGMCKR	138 116
	ConsensusLE.T ..GYL.D.L. WC....T...Y...C....C....N.V	200
	Human CD38 SM38p	QRDMFTIEDT LLGMLADDLT WCGEFNTSKI NYQS-QPDWR KDC--SNNPV LGVRCSLETI FPGYLFDELW CGNGSLGNT KYGTVCG--- CDYKSNVV	185 161
	Consensus	..FW...S...A..A....V.LNGS....F..N.TFG.. E...L....V	250
	Human CD38 SM38p	SVFIKTVSRR FAEAACDVH VMLNGRSKI FDKNSTFGSV EVHNQPEKV HAFWQSASAE YARRASGNIF VVLNGSVKAP FNENKTFGKI ELPLLKHPRV	235 211
	Consensus	Q.L.....H.....R..C.....EL.....I.F. C.....	300
	Human CD38 SM38p	QTLEAWVHG GRE-DSRDLC QDPTIKELES IISKRNIQFS CKNIYRPDKF QLTVKLVHS LEDVNNRQTC ESWSLQELAN KLNHSVIPER QIDDPLEFRH	284 261
	Consensus	.QC..NP...C.....TS ..	342
	Human CD38 SM38p	LCQVKNPEDS SC-----TS EI YQCIENPGKQ LCQFSASTRS NVETLLILFP LVICLTFYTS MN	300 303

MMNVILFLTL	SNIFVFNSAQ	HQINILSEIV	QSRCTQWKVE	HGATNISCSE	50
IWNSFESTILL	STHTKSACVM	KSGLFDDFVY	QLFELEQQQQ	QRHHTIOTEQ	100
YFHSQVMNII	RGMCKRLGVC	RSLETTFPGY	LFDELNWCGNG	SLTGNTKYGT	150
VCGCDYKSNV	VHAFWQSASA	EYARRASGNI	FVVLNGSVKA	PFNENKTFGK	200
IELPLLKHPR	VQQLTVKLVH	SLEDVNNRQT	CESWSLQELA	NKLNSVHIPF	250
RCIDDPLEFR	HYQCJENPGK	QLCQFSASTR	SNVETLLILF	PLVICLTFYI	300
SMN					303

Figure 16

ATGATGAAYG	TNATHYTNTT	YYTNACNYTN	WSNAAYATHT	TYGTNTTYAA	50
YWSNGCNCAR	CAYCARATHA	AYYTNYTNWS	NGARATHGTN	CARWSNMGNT	100
GYACNCARTG	GAARGTNGAR	CAYGGNGCNA	CNAAYATHWS	NTGYWSNGAR	150
ATHTGGAAYW	SNTTYGARWS	NATHYTNYTN	WSNACNCAYA	CNAARWSNGC	200
NTGYGTNATG	AARWSNGGNY	TNTTYGAYGA	YTTYGTNTAY	CARYTNTTYG	250
ARYTNGARCA	RCARCARCAR	CARMGNACYC	AYACNATHCA	RACNGARCAR	300
TAYTTYCAYW	SNCARGTNAT	GAAYATHATH	MGNNGGNATGT	GYAARMGNYT	350
NGGNGTNTGY	MGNWSNYTNG	ARACNACNTT	YCCNGGNTAY	YTNTTYGAYG	400
ARYTNAAYTG	GTGYAAYGGN	WSNYTNACNG	GNAAYACNAA	RTAYGGNACN	450
GTNTGYGGNT	GYGAYTAYAA	RWSNAAYGTN	GTNCAYGCNT	TYTGGCARWS	500
NGCNWSNGCN	GARTAYGCNM	GNMGNGCNWS	NGGNAAYATH	TTYGTNGTNY	550
TNAAYGGNWS	NGTNAARGCN	CCNTTYAAYG	ARAAYAARAC	NTTYGGNAAR	600
ATHGARYTNC	CNYTNYTNAA	RCAYCCNMGN	GTNCARCARY	TNACNGTNAA	650
RYTNGTNCAY	WSNYTNGARG	AYGTONAAYAA	YMGNCARACN	TGYGARWSNT	700
GGWSNYTNCA	RGARYTNGCN	AAYAARYTNA	AYWSNGTNCA	YATHCCNTTY	750
MGNTGYATHG	AYGAYCCNYT	NGARTTYMGN	CAYTAYCART	GYATHGARAA	800
YCCNGGNAAR	CARYTNTGYC	ARTTYWSNGC	NWSNACNMGN	WSNAAYGTNG	850
ARACNYTNYT	NATHYTNTTY	CCNYTNGTNA	THTGYYTNAC	NTTYTAYACN	900
WSNATGAAY					909

Figure 17